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Effects of β-, β1-, and β2-adrenoceptor agonist infusion on plasma non-esterified fatty acids in non-pregnant, non-lactating, underfed cows

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Catecholamine stimulation of lipolysis through adipocyte β-adrenoceptors (AR) is of major importance for the regulation of lipid mobilization from adipose tissue. The stimulation causes a serie of intracellular reactions that ultimately activate hormone-sensitive lipase and results in the breakdown of triglycerides into non-esterified fatty acids (NEFA) and glycerol. The rates of lipomobilization can been assessed from the changes in plasma NEFA concentration. The latter increased when the demand was enhanced by energy restriction. When injected or infused epinephrine or isoproterenol increased plasma NEFA concentration more into fasted or underfed than into well fed cattle (Fröhli and Blum, 1988, Acta Endocrinol, 118, 254-259; Bocquier and Chilliard, 1992, J Dairy Sci, 75, 236). Binding studies using β1- or β2-selective-AR antagonists demonstrated the existence of β1- and predominantly β2-AR subclasses in sheep and calf adipocytes (Bowen *et al*, 1992, Biochem Pharmacol, 44, 681-686; Van Liefde *et al*, 1994, Arch Int Pharm Thér, 327, 69-86). To our knowledge, *in vivo* administration of selective β1- and β2-agonists have not been performed in cattle. It could determine what part may play each β1- or β2-adrenergic component in lipolytic response. The purposes of this study were 1) to evaluate the activity of selective β1- (dobutamine, D) and β2- (terbutaline, T) agonists when compared with a nonselective β-AR agonist (isoproterenol, I) and 2) to establish the dose-response curves of the lipolytic effects of these compounds on plasma NEFA concentrations.

To maximize plasma NEFA responses to β-agonist infusion, three multiparous dry non-pregnant Holstein x Friesian cows were underfed at 60 % of maintenance energy requirements during 2 weeks. The diet consisted of 24.2 % of barley, 20.8 % of soybean meal, and 55.0 % of hay. The animals received daily 100 g mineral-vitaminic premix. Total mixed diet was offered at 11h30. Catheters were implanted in each jugular vein on the day before the start of a 5-day experiment. Each β-agonist was iv infused for 60 min at 9h30, five doses being tested on successive days in the same cow (1, 2, 4, 8 and 12 nmol/kg BW for the entire infusion). Blood samples were obtained at -5, +10, +20, +30, +45, +60 min relative to the start of infusion. Response areas of plasma NEFA were calculated as area under the response curve and above the baseline from zero to 60 min. Concentration at -5 min was used as baseline.

Isoproterenol induced similarly elevated plasma NEFA response areas whatever the infused dose. However, with T infusion the response was much lower at the lower doses. Response areas of plasma NEFA were similar with I and T at 8 and 12 nmol/kg BW infusions. There was no change in plasma NEFA in the range of D doses used, but D had null, small or high lipolytic effect for 30, 60 or 120 nmol/kg BW, respectively (results not shown).

Isoproterenol stimulated more lipolysis than T at very low doses. Selective β2-AR activation with doses of 4 or 8 nmol/kg BW of T enhanced lipolysis, whereas the stimulation of lipolysis with selective β1-AR agonist occurred at much higher doses. The differences in NEFA responses between nonselective β-, and selective β1- and β2-AR agonists could be explained by a lower β1- than β2-AR number in adult cattle adipose tissue, as was demonstrated in sheep (Bowen *et al*, 1992). Isoproterenol could present a stronger affinity for β-AR than T and D. A low affinity of D for β1-AR could have contributed to the lack of lipolytic effect at low doses. Differences in clearance rate, or indirect lipolytic effects through differences in stimulation of catecholamine secretion could also explain the differences observed between the 3 β-AR agonists (Lafontan *et al*, 1988, Reprod Nutr Dévelop, 28, 61-84; M Berlan, pers comm).

	infused doses				
(nmol/kg BW/60 min)	1	2	4	8	12
	NEFA response area (mM min)				
I	30.0	30.4	37.9	40.3	34.1
T	3.3	1.3	18.6	36.6	33.3
D	2.6	7.2	5.1	-2.4	-1.0